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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,817	10/29/2003	Eyal Raz	UCAL-292	1602

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,817	RAZ ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-17 and 24-27* is/are pending in the application.

4a) Of the above claim(s) *10,11 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-9,12-14,16,17 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication (RCE) filed 1/16/2008. The status of the claims is as follows: claims 1, 3, 4, 6-17 and 24-27 are pending. Claims 1, 3, 4, 6-9, 12-14, 16-17 and 24-27 are under current examination. The original election of species are as follows: idiopathic pulmonary fibrosis, 5'-(TCG)n-3' and systemically.

The Examiner previously stated some claims were allowable; this was in error. No claims were allowed.

The following rejection has been *withdrawn*:

1. 35 USC 112, 1st paragraph (Scope of Enablement). Briefly, the rejection was drawn to CpG sequences and whether there would be any undue experimentation by the skilled artisan in making them. Applicants presented a persuasive argument and this rejection is withdrawn.

Claim Objections

Claim 6 is objected to because of the following informalities: 5'-(TCG)n does not contain the -3' . Appropriate correction is required.

Specification

The use of the trademark MUSCOMYST and others has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. See for example page 40.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112-NEW

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, 6-9, 12-14, 16-17, 24-25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are drawn to a method of treating a lung fibrosis in an individual, more specifically, idiopathic pulmonary fibrosis.

State of the prior art. Moore and Hogaboam (2008) review the differential murine models of pulmonary fibrosis. While the authors state that animal models have led to the identification of a number of key cells, mediators, and processes that are likely involved in human fibrosis (see Introduction), there is no current model (2008) that recapitulates all of the cardinal manifestations of the human disease (see Abstract). Table 1 provides the advantages and disadvantages of 7 various animal models of

fibrosis. It is interesting to note that administration of OVA, an allergen, is not among them. Table 2 demonstrates the fidelity of animal models of fibrosis to humans. Among the cardinal manifestations of this disease (see last paragraph), humans and animal models are incongruent for the following: acute inflammation, chronic inflammation and temporal heterogeneity (which suggests sequential, multiple injuries; see Introduction). Further emphasized is that chronic inflammation is variable in humans but is definite in animal models.

Gross and Hunninghake (2001) review the medical progress of idiopathic pulmonary fibrosis. See Figure 2 which depicts the “Original Hypothesis” and the “New Hypothesis” for the pathogenesis of idiopathic pulmonary fibrosis. Note that the New Hypothesis no longer shows chronic inflammation of the lung as a cause of this disease. Page 518 addresses this directly and the authors state the following “it is now clear that current anti-inflammatory therapy for idiopathic pulmonary fibrosis provides no benefit”. Again, they state the “When anti-inflammatory agents were given only to patient with a secure diagnosis of idiopathic pulmonary fibrosis, there was no evidence of a meaningful response" (see page 522). The authors also state the following: "At present, there are no proven therapies for idiopathic pulmonary fibrosis” (see page 522). Lastly, the authors state the following: “Given the poor prognosis associated with idiopathic pulmonary fibrosis, patient should be referred to regional centers of expertise for enrollment in therapeutic clinical trials or for lung transplantation” (see page 523).

In sum, the prior art provides that this disease has a poor prognosis in patients, chronic inflammation is not associated with its cause, anti-inflammatory therapy

provides no benefit and there is no absolute animal model. Note that Moore and Hogaoam state that chronic inflammation is variable in UIP, which encompasses a number of pathologically distinct categories (see Introduction of Gross and Hunninghake).

Breadth of the claims. The claims are broad in that they drawn to treating interstitial lung fibrosis which may encompass all of those found in claim 4, including chronic exposure to an irritant, chronic bacterial infections and other chronic disease states.

Working examples. The working examples support a chronic asthmatic model in that the mice were repetitively challenged with OVA. Administration of ISS modulates the effects of OVA. It is not clear how the examples are of idiopathic pulmonary fibrosis.

Guidance in the specification. There is none. Applicants nebulously mention the bleomycin model in a hypothetical a couple of times (eg paragraph 66) but no real data is provided. There is guidance for chronic asthma and actual to support its treatment but not for idiopathic pulmonary fibrosis. Applicant is invited to point out where specific steps are for treatment.

Predictability in the art. A treatment cannot be predicted. The prior art has shown that that this disease has a poor prognosis in patients, chronic inflammation is not associated with its cause, anti-inflammatory therapy provides no benefit and there is no absolute animal model. Thus, one could not simply mimic the treatment for chronic asthma and expect for it to work on this disease.

Amount of experimentation necessary. Given there no working examples providing any data at all, the ordinary artisan would be required to begin at square one, that is, generating data. The artisan would be required to administer ISS to multiple animals of different accepted models, calculate the effective doses, if effective at all, and ascertain the results over and over until a sufficient amount data is collected. It is not clear whether the results will demonstrate a successful treatment, as the Applicants so optimistically claim. This would take years. As discussed above regarding the prior art, there are many issues to be worked out.

For the reasons above, it would require undue experimentation for one skilled in the art to make and use the method as claimed.

Claim Rejections - 35 USC § 102-NEW

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 6, 78, 12, 25 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Kline et al (2002).

Kline et al describe the treatment of "established asthma" in a murine model using CpG-oligos (see whole document). Figure 1 demonstrates the murine model of asthma induced by OVA and the immunotherapy protocol (also see the corresponding figure legend). The authors state: "To model persistent asthma in humans, who, by current standards of treatment, require intensive anti-inflammatory therapy, we next

treated mice with established airway eosinophilia (see page 172). Of note, the eosinophilic inflammation was well established before the initiation of therapy. The ODNs administered are found on page 171. The authors show that CpG ODN were most effective in preventing aspects of atopic inflammation when administered in conjunction with antigen, rather than alone, suggested that CpG ODN may be an effective adjuvant for immunotherapy (see Discussion). In conclusion, the authors state the following: "Current thought on the management of asthma, as epitomized in the recent National Heart, Lung, and Blood Institute (NHLBI) asthma guidelines, has stressed anti-inflammatory therapy as the cornerstone of asthma treatment. The genesis of this approach is that reduction of inflammation should lead to diminished airway remodeling and thus less long-term asthma sequelae" (see last paragraph, page 178). The authors conclude that the addition of CpG DNA as an adjuvant for immunotherapy may substantially enhance its usefulness for the management of allergic disease (see page 178).

Double Patenting-MAINTAINED

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6-9, 12-13 and 24-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 15 of U.S. Patent No. 6498148. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method steps from both sets of claims involve the same population of individuals and the same product is administered, thus resulting in the same inherent effect. Applicants will consider filing a Terminal Disclaimer. Thus, this rejection is maintained.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/
Examiner, Art Unit 1648

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648